MED
T113
+Y12
6641

YALE UNIVERSITY LIBRARY
39002010063759

COMPLICATIONS IN PREVIOUSLY IRRADIATED SALVAGE MASTECTOMY PATIENTS

Jennifer Chiu

YALE UNIVERSITY

1999

YALE
UNIVERSITY

CUSHING/WHITNEY
MEDICAL LIBRARY

Permission to photocopy or microfilm processing of this thesis for the purpose of individual scholarly consultation or reference is hereby granted by the author. This permission is not to be interpreted as affecting publication of this work or otherwise placing it in the public domain, and the author reserves all rights of ownership guaranteed under common law protection of unpublished manuscripts.

Signature of Author

5/2/99

Date

Digitized by the Internet Archive
in 2017 with funding from
Arcadia Fund

https://archive.org/details/complicationsinp00chiu

Complications in Previously Irradiated Salvage Mastectomy Patients

A Thesis Submitted to the
Yale University School of Medicine
in Partial Fulfillment of the Requirements for the
Degree of Doctor of Medicine

by
Jennifer Chiu
1999

Med Lib
T113
+Y12
6641

YALE MEDICAL LIBRARY
AUG 17 1999

Presented at the New England Cancer Society
November 1996
Dartmouth-Hitchcock Medical Center

Awarded the Resident's Award for Excellence in
Clinical Research

TABLE OF CONTENTS

PAGE

1. Acknowledgements...4

2. Abstract...5-6

3. Introduction...7-15

4. Materials and Methods...16-17

5. Results...18-22

6. Discussion...23-28

7. Bibliography...29-31

GRAPHS

Graph 1: Breast cancer cases in Connecticut.. 8

Graph 2: A comparison of salvage mastectomy patients versus nonirradiated control patients...18

Graph 3: Types of complications in salvage mastectomy and primary mastectomy patients...19

Graph 4: Complication rates in patients who elected to have reconstruction versus those without reconstruction...............22

TABLES

Table 1: Types of therapy employed in the treatment of breast cancer recurrence in the studied population of 67 patients.16

Table 2: Types of complications in salvage mastectomy versus primary mastectomy patients...19

Table 3: Further breakdown of salvage mastectomy patients (modified versus radical)...20

I would like to acknowledge the invaluable support and guidance of my thesis advisor Dr. Barbara Ward as well as Dr. Bruce Haffty and Dr. Richard Restifo. I would also like to acknowledge the help of Dr. Doug Forman and extend my thanks to Maureen Lillis and the assistant in the surgery department who so patiently helped me with my slides. And, to my family and friends, thanks always.

In addition, many thanks to the Office of Student Research at Yale University School of Medicine for summer funding of this research project.

ABSTRACT:

COMPLICATIONS IN PREVIOUSLY IRRADIATED SALVAGE MASTECTOMY PATIENTS. Jennifer Chiu, Bruce Haffty, Richard Restifo, and Barbara Ward. Section of Surgical Oncology, Department of Surgery, Yale University, School of Medicine, New Haven, CT.

Prior studies show a wide range of complication rates varying from 7 to 28% in previously irradiated salvage mastectomy patients. In addition, the suitability of implant reconstruction versus autologous tissue reconstruction has not been shown definitively in these patients. This study retrospectively reviewed a group of 1040 patients treated with lumpectomy and radiation therapy at Yale prior to 1990, of which we reviewed the charts of 67 patients, ages 31-80 (average age 51.5 years) who had a breast cancer recurrence. An unmatched control consisted of 25 patients whose primary treatment was mastectomy without prior irradiation.

Of the 67 previously irradiated patients, 57 had salvage mastectomies for their recurrences. The complication rate was 47% among this group versus 28% in the non-irradiated control group. In both groups, seromas were the most common form of wound complication (9/57 and 3/25) followed by cellulitis (7/57 and 1/25). Of note, some of the seromas took weeks to resolve in the irradiated group.

Of the patients who had salvage mastectomies, 9 patients (10 breasts) underwent a two stage prosthetic reconstruction. The average follow up was 5.1 years. The mean dose of radiation was 6,070 cGy, and the average interval from radiation therapy to placement of the tissue expander was 4.6 years. In one patient (10%) the tissue expander extruded. In four reconstructions (40%) there was an uneventful course. Two cases (20%) were difficult to expand and the final result lacked projection. One patient (10%) developed an infection requiring removal of the permanent prosthesis. Two patients (20%) developed Baker class III or IV capsular contractures. Overall, in this group of patients with implant reconstruction, 60% of the reconstructions resulted in either a complication or an unfavorable result. Of four patients who opted for TRAM flap reconstruction, one of four had the complication of fat necrosis.

These results suggest that previously irradiated salvage mastectomy patients are at a higher risk for postoperative complications than are non-irradiated mastectomy patients. In addition, this study provides evidence that there may be fewer complications with immediate TRAM flap reconstruction than with immediate tissue expander reconstruction, making it the recommended form of reconstruction for this group of patients.

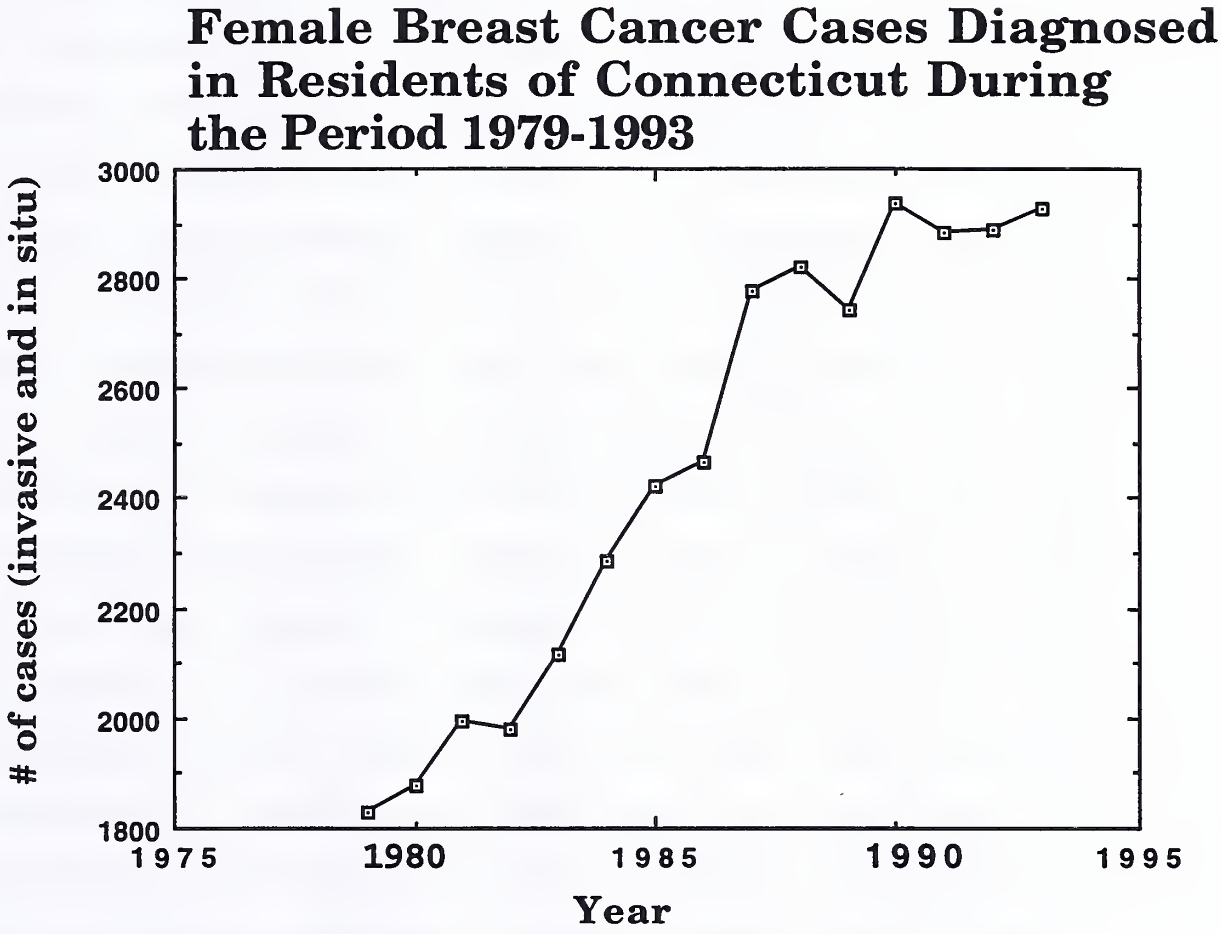
INTRODUCTION:

The incidence of breast cancer, the most common cancer in North American women, has risen at an annual rate of 1.2% since 1940. Between 1982 and 1986, the rate of increase was 4% per year. Since 1940, breast cancer mortality has also increased, but more slowly. In fact, breast cancer mortality has been stable since 1950, but this figure masks a 15% increase among women 55 years of age and older and a concomitant 15% decrease among those younger than 55.[1] An estimated 183,000 American women were diagnosed with breast cancer in 1994, and an estimated 46,300 were predicted to die. It is the leading cause of death among American women, aged 40-55.[2]

The disparity between a rapid rise in incidence and a modest increase in mortality is not easily explained. Part of the reason may be increased registration of the disease and widespread use of mammography in recent years. Prior to the 1980's, <15% of women had regular screening. Many of the cancers now being diagnosed are of the in situ variety, and it is uncertain whether all of these tumors would go on to become invasive if left undiagnosed. Another reason may be the apparently less aggressive character of many of the newer invasive tumors. Finally, improvements in treatment, especially in the past 30 years, may have partially counterbalanced the increase in incidence.[2]

In Connecticut, the incidence of breast cancer has risen steadily over past 2 decades, reflecting an aging population, improved

imaging modalities, and higher awareness and compliance with screening.



GRAPH 1: Breast cancer cases in Connecticut: This graph illustrates the sharp rise in breast cancer cases over the past two decades. This rise reflects both an aging population as well as earlier diagnosis with better imaging modalities. Lead-time bias is evidenced by the recent plateau in breast cancer cases beginning in 1990, reflecting a stabilization in the use of screening.

Incidence rates underestimate the number of women who are affected by this disease in one way or another though. For every woman who is diagnosed with breast cancer, another five will undergo breast biopsy. It is likely that over 20 million American women will see their physician this year about a potential breast cancer.[2]

Currently the cumulative risk for any American woman developing breast cancer is 12%.[2] The single most important risk factor is age, especially in Western countries. The probability that a 60-year-old white American woman will develop breast cancer in a single year (1 in 420) is fourteen times that of a 30-year-old (1 in 5900). At least two hereditary patterns can be ascertained, one with a familial aggregation associated with a modest increase in risk and the other a truly genetic pattern with high penetrance and linkage to a specific gene. Although any family history of breast cancer is associated with an increase in risk, only a history of breast cancer in a first-degree relative (parent, sibling, or child) is associated with more than a trivial increase. A woman's relative risk of developing breast cancer is 1.8 if only her mother had breast cancer, 2.5 if one sister had breast cancer, and 5.6 if both her mother and one sister had breast cancer. Genetic breast cancers occur at a younger age, are more likely to be bilateral, and appear in multiple family members over three or more generations. Specific genes linked to these cancers have been identified on chromosome 17 and include the p53 and the BRCA1 gene. The discovery of these genes opens up the possibilities of identifying women at high risk for breast cancer, but at present genetic screening is inappropriate unless a woman has a pedigree highly suggestive of genetic breast cancer.

A woman with a history of breast cancer, whether in situ or invasive, has an increased risk of approximately 0.5-1% per year of developing a new breast cancer in any remaining breast tissue. This risk is not entirely proportional to the amount of breast tissue

removed. Fortunately, two breast cancers, whether concomitant or sequential, do not impart a worse prognosis than one breast cancer.

Some types of benign breast disease carry an increased risk of breast cancer. For example, atypical hyperplasia has a relative risk for breast cancer of 4.4. Other risk factors for breast cancer include endogenous endocrine factors such as longer intervals from menarche to the first full-term pregnancy and from menarche to cessation of menses. Women whose menarche begins at age 12 or earlier have twice the risk of developing breast cancer as those whose menarche begins after age 13. Women who have a natural menopause after age 55 are at twice the risk of developing breast cancer as those with a natural menopause prior to age 44. The increased risk associated with the use of estrogen replacement therapy (ERT) in postmenopausal women or oral contraceptives in premenopausal women is either very small or nonexistent. However, prolonged use of these therapies may result in a modest increase. In a meta-analysis of ERT studies, the relative risk of developing breast cancer was 1.3 among women taking ERT for >15 years.[5] The risk seems to be somewhat greater if estradiol, rather than conjugated estrogens, is used and if ERT is begun during the menopausal years. The use of progestins with ERT does not decrease, and may even augment, the risk of developing breast cancer. A meta-analysis of oral contraceptive studies failed to demonstrate any association between oral contraceptive use and overall risk of developing breast cancer, but prolonged use, especially prior to the first full-term pregnancy, was associated with an increased risk of developing breast cancer before age 45.[6] The relative risk from oral

contraceptive use for >10 years was 1.46 (P=.001) and the relative risk from oral contraceptive use for 4 years prior to the first full-term pregnancy was 1.72.[2]

There are large regional differences in the incidence of breast cancer. In the San Francisco bay area, the annual incidence among whites is 87 per 100,000 in contrast to only 18.6 per 100,000 in rural Japan. Incidence studies among migrants who move from low- to high-incidence areas have demonstrated that the risk of developing breast cancer in the migrant population will gradually rise to the level of the population in the new locale. This pattern of change suggests a role for environmental factors in the etiology of breast cancer. Among the environmental factors studied so far, a region's total production of dietary fat is most closely associated with breast cancer risk.[7]

The dietary factor most consistently shown to be associated with an increased risk of breast cancer is alcohol intake. A meta-analysis of epidemiological studies demonstrated that an alcohol intake of 6 g/day (about 1/2 drink) may be associated with a relative risk of 1.3; and intake of 36 g/day was associated with a relative risk of 2.[8]

Two of the most striking features of breast cancer are its variable behavior in different patients and its relatively slow growth rate compared with other tumor types. The median survival of patients who decline all forms of treatment is about 2.8 years, but the tail of these curves is quite long, with some patients living 15-20 years. Doubling time of the tumor varies from a few days to >2000 days (mean 100 days), and most patients with the diagnosis of breast

cancer will have had the disease for 5-10 years prior to diagnosis. Less than one-third of the patients with a diagnosis of breast cancer will die of this disease, and the majority of those cured will have benefited from local treatment alone.

With the increased awareness of the psychological impact of a mastectomy, conservation of the breast has gained emphasis in the management of breast cancer. More extensive surgery, such as the Halsted radical mastectomy, has been largely abandoned as multiple randomized trials have now demonstrated that the 10-20 year survival of patients treated with lumpectomy and radiotherapy is equivalent to that achieved with mastectomy or mastectomy plus adjuvant radiotherapy.[9] With its relative effectiveness and cosmetic and psychological advantages, breast-conserving therapy is standard therapy for primary treatment of stage I and II breast carcinomas, as recommended by the 1990 National Institutes of Health Consensus Development Conference.[10] Conservative therapy usually includes breast-conserving surgery and radiation therapy to eliminate microscopic foci. There is a 1-2% per year actuarial risk of local recurrence following conservative therapy and a long term failure rate of 15-20%.[11]

To control recurrent tumor growth, salvage mastectomy, followed by the appropriate systemic therapy, has become a viable, effective treatment. Improvements in surgical technique and postoperative management have led to a reduction in the morbidity, mortality, and recurrence associated with aggressive surgical treatment of recurrences. Published series following salvage

mastectomy have identified a number of factors that may influence the risk of subsequent distant relapse, including disease-free interval,[12,13] initial tumor stage,[14] histology of the recurrent tumor,[15] and patient age.[16] The 5 year actuarial risk of recurrence following salvage mastectomy in one series was 41%,[16] with histology influencing risk of recurrence most substantially; predominantly invasive tumors were found to be associated with a higher risk (5 year 52% crude risk) of relapse than focally invasive or non-invasive tumors (0/24 patients with relapse). The five year survival of patients in the abovementioned series ranged from 53-81%.[12-16] The extent of recurrence in the breast was found to be associated with the risk of further distant failure in the series by Kurtz et. al.[12] and Haffty et. al. [17], while Clarke et. al.[18] noted that nodal or dermal recurrence was associated with poor overall survival. Haffty et. al.[19] investigated the prognostic significance of DNA flow cytometry of the recurrent tumor and defined a favorable group based on DNA ploidy and S-phase fraction. To date, no published series has shown a statistically significant improvement in subsequent outcome with the administration of chemotherapy or hormonal intervention. However, demonstration of such an effect in a retrospective analysis is difficult due to the small number of patients and the nonrandom application of such therapy.

While patients who undergo salvage mastectomy after a recurrence in the breast following conservative therapy(CT) and radiation therapy(RT) are at substantial risk of further relapse, their prognosis appears to be better than that of women who have chest wall recurrence after initial mastectomy. 59% of those who have a

recurrence in the breast following CT and RT are disease-free 5 years after salvage mastectomy.[16] In contrast, only 30% of patients who develop a chest wall recurrence after initial mastectomy are disease-free at 5 years.[20]

Surgery of previously irradiated areas poses problems of wound healing secondary to radiation-induced damage. In 1975, Robinson[21] proposed mechanisms by which radiation-induced changes occur: microvascular endarteritis, excessive fibrosis, and chromosomal alteration. Following initial ionization, cells are killed or severely defunctionalized resulting in a red, dry, braised appearance to the skin, the severity of changes being related to the source, intensity, and length of time of the radiation dosage.

Soon after heavy radiation, the skin may show varying degrees of necrosis, but usually, within a few days or weeks, it will have appeared to have recovered. The superficial and deep changes continue to progress, however, because of the inexorable progress of the induced endarteritis obliterans. The change in the small blood vessels, and even in larger ones, is the primary factor influencing later tissue defects. Excessive fibrosis is the second fundamental change (scar is notorious for its poor wound healing qualities). The third factor is the direct cellular damage with chromosomal alteration, which may prevent further cellular replication in a normal manner.

The changes in small blood vessels, scar, and cellular damage all contribute to increased wound complications, making surgery of radiation-exposed tissue a challenge. The general principles are to 1) remove altered tissues to the level of good minute blood supply, and

2) to provide suitable coverage. The coverage is as good as the blood supply that supports it, and because progressive diminution of the blood flow in the altered tissues is a fundamental problem, resection of an area large enough to obtain margins with a healthy blood supply is necessary. Otherwise, progressive postoperative necrosis may be expected, with infection and poor wound healing.

MATERIALS AND METHODS:

Of 1040 patients treated at Yale Hunter Radiation Therapy Center, with a lumpectomy and radiation therapy between 1975 and 1990, 92 patients had a local ipsilateral recurrence following conservative therapy. We reviewed the charts of 67 of these 92 patients. Of the 67 patients, 57 elected to undergo salvage mastectomy, and this group became the study population.

67/92 patients were followed up	
57	Salvage mastectomy
1	Prednisone therapy
3	Biopsy only
4	Wide local excision
1	Axillary sampling
1	Hyperthermia therapy

TABLE 1: Types of therapy employed in the treatment of breast cancer recurrence in the studied population of 67 patients.

43 of the 57 patients had a simple mastectomy, and 14 had a modified radical mastectomy. Demographically, the age ranged from 31-70, with a mean age of 51.5. Mean follow-up after first diagnosis, as of 1995, was 12.1 years. Mean survival time was 7.7 years, and mean time to breast recurrence was 4.8 years. Patients were treated with radiation in the range of 5200-6600 rads.

We also reviewed the charts of an unmatched control group of patients, consisting of 25 patients whose primary treatment was mastectomy without prior irradiation. Demographically, the age of

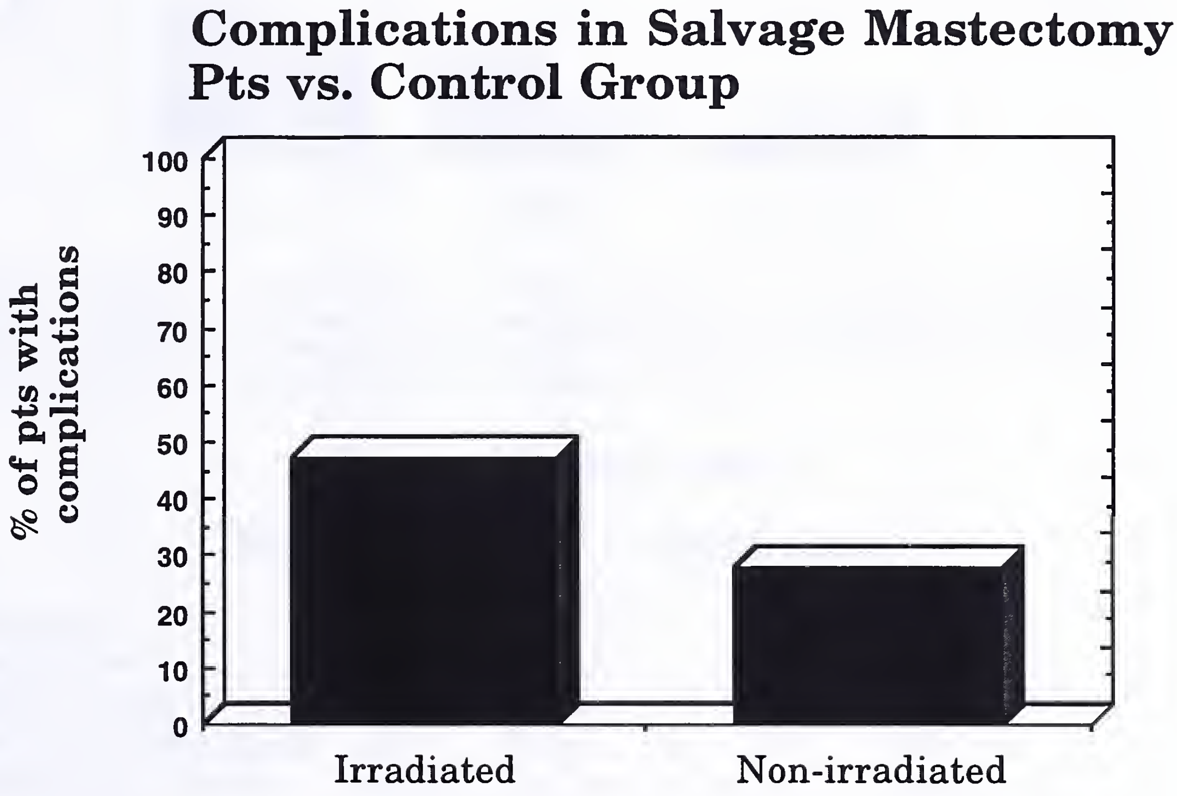
this group of patient ranged from 32-64 years of age (mean age 45.5).

15 patients elected to have reconstruction following the salvage surgery. 9 patients (10 breasts) opted for reconstruction with a submuscular tissue expander, which was replaced with a permanent prosthesis during a second stage. 4 patients chose immediate reconstruction with a TRAM flap, and two elected postponed reconstruction with a latissimus dorsi flap. The average age of the patients undergoing reconstruction was 47.9 years. 5 of the 9 patients undergoing implant placement were smokers. The mean dose of radiation to these patients was 6,070 cgy. 4 patients received chemotherapy following their salvage mastectomy. The average interval from completion of the radiation therapy to placement of the tissue expander was 4.6 years.

Capsular contracture complications were evaluated using the Baker grading system. Contracture significant enough to require implant removal was defined as Baker grade III or IV.

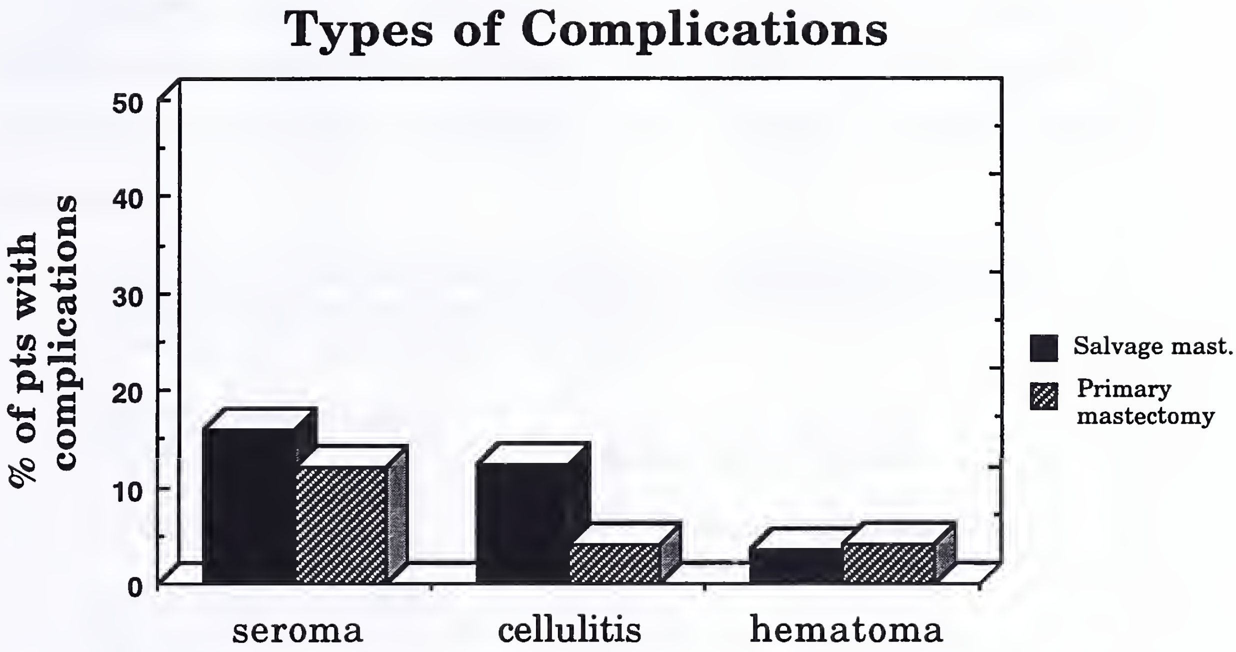
RESULTS:

Of the 57 patients who had a salvage mastectomy to treat their recurrences, the complication rate was 47% among these patients versus 28% in the non-irradiated group of 25 patients.



GRAPH 2: A Comparison of salvage mastectomy patients versus nonirradiated control patients: 22/57 salvage mastectomy patients experienced postoperative complications versus 7/25 nonirradiated mastectomy patients.

In both groups, seromas were the most common form of wound complication followed by cellulitis.



GRAPH 3: Types of complications in salvage mastectomy and primary mastectomy patients. 15.8% and 12% of patients in the salvage mastectomy and primary mastectomy groups, respectively, had seromas. 12.3% and 4% of patients respectively had cellulitis. 3.3% and 4% of patients respectively had hematoma formation.

Types of Complications

	Salvage mast.	Mastectomy
Seroma	**9**	**3**
Cellulitis	**7**	**1**
Hematoma	**2**	**1**
Swelling of the axilla	1	0
Pleural effusion	1	0
Arm edema	1	0
Brachial plexus stress injury	1	1
Wound debridement/necrosis	0	1

TABLE 2: Types of complications in salvage mastectomy versus primary mastectomy patients: The total number of patients with complications was 22 and 7 in the two groups. Seromas comprised 40.9% of complications in the salvage mastectomy group and 48.9% of complications in the primary mastectomy group. Cellulitis comprised 31.8% and 14.3% of complications in the two groups, respectively, and hematoma formation comprised 9.1% and 14.3% of complications in the two groups respectively.

Outlined below is a further breakdown of complications in patients who had salvage mastectomies without reconstruction. Of these 43 patients, 29 patients had a simple mastectomy, and 14 had a modified radical mastectomy.

SALVAGE MASTECTOMIES WITHOUT RECONSTRUCTION
43 patients had salvage mastectomy without reconstruction
20 patients of 43 had complications (46.5%)

29 simple mastectomies		
Complications:	12 patients of 29 (41.4%)	
No complications	17	(Thickening; induration 2 loose skin 1
Diffuse discomfort/pain	5	
Swelling of axilla	1	
Cellulitis	4	
Seroma	5	
Hematoma	1	

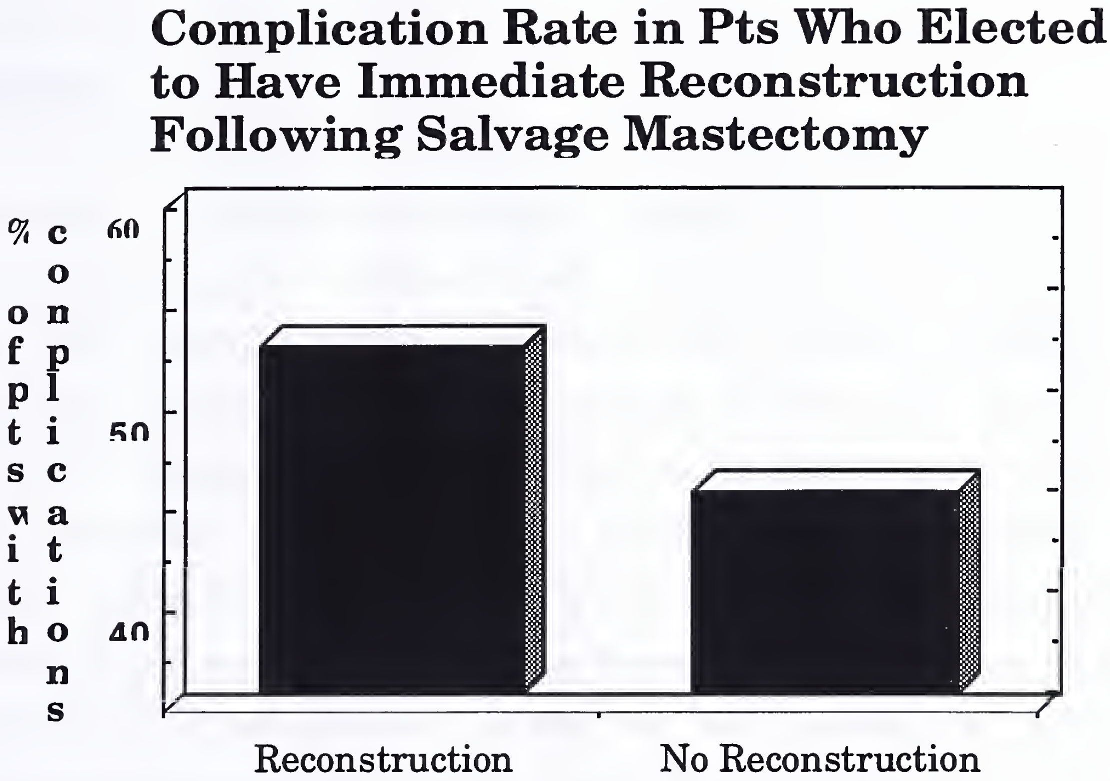
14 modified radical mastectomies		
Complications:	8 patients of 14 (57.1%)	
No complications	6	(loose tissue 1 dry skin 1)
Seroma	4	
Brachial plexus stress injury; dyesthesia	1	
Arm edema	1	
Cellulitis	3	
Shoulder discomfort	1	
Hematoma	1	

TABLE 3: Further breakdown of salvage mastectomy patients (modified versus simple mastectomy).

The 12 patients (13 breasts) who had reconstruction had a higher rate of complications than the patients who did not have reconstruction. 1 of the 4 patients with immediate TRAM flap

reconstruction had an area of fat necrosis. In one patient the tissue expander extruded 1 month after insertion. In the other 8 patients (9 breasts), the mean duration from the placement of the tissue expander to placement of the permanent prosthesis was 6 months (range-3 to 11 months). The following types of permanent implants were placed: two textured saline, and four double lumen (Heyer Schulte) implants.

The average follow up was 5.1 years. In 3 patients (4 breasts) the postoperative course was uneventful. In 2 patients there was an inability to expand the irradiated tissue adequately, and in both instances the final breast reconstruction lacked projection. One patient developed an infection that required removal of the permanent prosthesis 3 months after placement. This patient went on to have a TRAM flap reconstruction 5 months later. Two patients developed Baker class III or IV capsular contractures, both of whom had subsequent revisions. Of the 8 patients (9 breasts) eventually having a permanent prosthesis placed, 4 reconstructions (44.4%) required additional surgical revisions aside from the planned exchange of the tissue expander to a permanent prosthesis. Reasons for reoperation included deformed expansion requiring repositioning of the tissue expander in 2 patients, and capsular contracture requiring capsulectomy and implant exchange in 2 patients.



GRAPH 4: Complication rates in patients who elected to have reconstruction versus those without reconstruction: 8 of 15 patients who had reconstruction (53.3%) had complications versus a complication rate of 47% in the nonirradiated group.

Of the two patients who elected to have autologous tissue reconstruction with a latissimus dorsi flap and implant, One patient had an area of partial flap necrosis. Of the 4 patients who had TRAM flap reconstruction, one patient had an incidence of fat necrosis.

DISCUSSION:

Previously irradiated patients are at a higher risk for postoperative complications, in particular seromas and cellulitis (16% and 12% respectively, as compared with 12% and 4% in the control group.) The literature reports complication rates following salvage mastectomy in previously irradiated patients in the range of 7-24%.[22-24] The complication rate of 47% in the irradiated group and 29% in the control group in our study is higher than in previously reviewed literature, and this may be the result of overzealous reporting in our study. In a series by Osborne et. al.,[22] only a 7% complication rate was obtained, a rate that they reported did not appear to be different from reported complication rates associated with mastectomy in non-irradiated tissue. (Of 46 pts, there was one wound infection, one hematoma, and one incidence of flap necrosis.) In a series of 25 salvage mastectomy patients by Barr et. al.,[23] 6 patients (24%) had wound infection or breakdown, one of whom required a split-skin graft to repair the defect due to skin edge necrosis. In a third series by Cacujum et. al., [24] 25 patients with salvage mastectomy were found to have a 15% rate of small wound complications, with 3 seromas and 1 delay in wound healing.

There was only a small difference, in the number of complications seen between patients electing modified radical vs. simple mastectomy for treatment of recurrence (57.4% vs. 41.1%, respectively). There was no increase in frequency of complications secondary to damage to lymphatic drainage (e.g. lymphedema or

increased infection) in the modified radical versus the simple mastectomy patient population.

Reconstruction in salvage surgery patients resulted in much higher rates of complications in the reviewed literature. In one series by Hathaway et. al.,[25] salvage surgery of 15 patients, 46.7% requiring chest wall resection, and all receiving either TRAM, latissimus dorsi, or omental flap reconstruction, resulted in a complication rate of 60%. This rate was divided into 40% minor complications (small wound problems) and 60% major complications (life-threatening events or major reoperative events.) Despite the complication rate, outcome supported the use of aggressive surgical treatment and reconstruction in patients with locally advanced and recurrent breast cancer.

The tissue expander with subsequent permanent implant placement has been used often and effectively for breast reconstruction. In a two stage reconstructive process, the tissue expander is placed to stretch the overlying tissue with the eventual goal of placing a permanent gel or silicone implant in its place. Previous literature has suggested that there may be difficulty in expanding previously irradiated skin and in the placement of submuscular implants. In a 1987 study, Dickson and Sharpe[26] reported only 3 of 10 implant reconstructions in previously irradiated patients progressed without complication. In 1995, Evans et al[27] reported that 4 of 7 implants placed with preoperative radiation therapy had complications. The complications included rupture, pain, or implant exposure, with removal of three of four implants. (1 Surgitex, 1 Becker, 1 saline, and 1 Siltex) Overall,

complications appeared unrelated to implant type (although polyurethane implants may be more resistant to radiotherapy) or the interval between implant placement and radiotherapy. Of note though, the authors excluded tissue expanders from their study, while, at present, in both the radiated and nonradiated patient, tissue expanders with or without flaps are performed more commonly than implant reconstructions alone.

Spear and Maxwell[28] suggested that two-stage (expander and then implant) textured anatomic saline implant reconstructions in radiated patients may perform better in a "capsulogenic" (likely to have capsular contracture) environment than smooth silicone gel-filled implants. There has also been ample evidence in other studies[28] that there is a lower rate of capsular contracture in saline-filled implants as compared with silicone-gel filled ones. Spear and Maxwell reported the successful use of two-stage textured saline expanders and implants in 10 of 10 patients with preoperative radiation where the skin was thought to be relatively healthy, stressing the importance in assessing the quality of the soft tissues and the extent of radiation damage.

In the group of patients undergoing staged tissue expander and implant reconstructions in our study, a favorable result was achieved in only 40% of patients. 60% resulted in either a complication or an unfavorable result. These results are consistent with the previously mentioned studies of implant placement in irradiated tissue and suggest that the scar and fibrosis in the area of the irradiated tissue make satisfactory expansion difficult.

The success of surgery depends highly on the quality of the tissue. Reconstruction with autologous tissue is more likely to give better cosmetic results and a lower complication rate. In addition, reconstruction with the TRAM flap often is more effective than reconstruction with the latissimus dorsi flap because more irradiated tissue is replaced.[28] The TRAM flap has outstanding vascularity as well with the hypogastric artery supply to the muscular pedicle. The complication rate for TRAM flap reconstruction in our group of patients was 25%, (1/4 - fat necrosis.) Of the two latissimus dorsi flap and a silicone gel implant reconstructions, one patient had a flap loss greater than 10%, resulting in a complication rate of greater than 50% for this technique. This rate of complications in previously irradiated autologous tissue reconstruction is consistent with the study by Kroll and colleagues[29] in which there was a 39% complication rate among previously irradiated patients versus 25% in nonirradiated patients. TRAM flap patients had a 33 and 21% complication in previously irradiated and non-irradiated patients respectively. 63% of latissimus dorsi patients that were previously irradiated versus 41% in the nonirradiated group had complications. Although our study is consistent with previous evidence that breast reconstruction in previously irradiated tissue, even when autologous tissue is used for reconstruction, is associated with a higher rate of complications, it should be noted that fat necrosis, the complication in our study, is more a result of inadequate donor blood supply than of the preexisting irradiated tissue.

Three of the patients in our study underwent prophylactic mastectomies on the opposite breast followed by staged

reconstruction bilaterally, using the same type of implant on both breasts. When compared by Dr. Forman[30] with the nonirradiated side in two patients, the irradiated breast had less projection, and was markedly firmer in the third patient (Baker Class III capsular contracture). Fodor and Swistel reported on the inability to expand fully the implant in a previously irradiated salvage mastectomy patient,[31] despite supposedly adequate volume within the implant. They documented with computed tomography that the tissue expander created a bony chest wall deformity due to the unyielding nature of the irradiated soft tissue. Both of the patients in our study had their implants filled to capacity. Whether there were compensatory bony changes in these patients was uncertain.

No correlation could be made between the type of permanent prosthesis and the outcome. In addition there was no trend noted between smoking, the time interval from irradiation to placement of the tissue expander or postoperative chemotherapy, and the eventual result of the implant reconstruction.

Most patients were irradiated during the mid 1980's and many of the implants used are now outdated. With refinements in radiation therapy and improved prosthetic devices, greater success with implant reconstruction may be possible.

As noted in previous studies, patients who originally opted for breast-sparing treatment with radiation therapy for their initial breast cancer, have a large potential for postoperative complications following salvage surgery. Consequently, the patient needs to be informed of the potential for adverse outcome with salvage mastectomy and with either implant or autologous tissue

reconstruction. Autologous tissue reconstruction was associated with much better cosmetic results and outcome in this study than tissue expander-implant reconstruction, making it the recommended method of reconstruction for this population of salvage surgery patients.

BIBLIOGRAPHY

1. Harris JR, Lippman, ME, Veronesi U, Willett W. Breast Cancer. NEJM. 327: 319-328, 390-398, 473-480, 1992.

2. Murphy, G, Lawrence, W, Lenhard, R, ed. The American Cancer Society Textbook of Clinical Oncology. American Cancer Society; 198-219, 1995.

3. Steinberg KK, Thacker SB, Smith SJ, et al. A meta-analysis of the effect of estrogen replacement therapy on the risk of breast cancer. JAMA. 265: 1985-1990, 1991.

4. Romieu I, Berlin JA, Colditz G. Oral contraceptives and breast cancer: review and meta-analysis. Cancer. 66: 2253-2263, 1990.

5. Prentice, RL, Kakar, F, Hursting S, Sheppard L, Klein R, Kushi LH. Aspects of the rationale for the Women's Health Trial. J Natl Cancer Inst. 80: 802-814, 1988.

6. Howe GR, Hirohata T, Hislop TG et al. Dietary factors and risk of breast cancer: combined analysis of 12 case-control studies. J natl cancer Inst. 82: 561-569, 1990.

7. Willett WC, Stampfer MJ, Colditz GA, Rosner BA, Henekens CH, Speizer FE. Dietary fat and the risk of breast cancer. N Engl J Med. 316: 22-28, 1987.

8. Longnecker MP, Berlin JA, Orza J, Chlamers TC. A meta-analysis of alcohol consumption in relation to the risk of breast cancer. JAMA. 260: 652-656, 1988.

9.Harris JR, Recht A Conservative surgery and radiotherapy. In: Harris JR, Hellman S, Henderson IC, Kinne DW, eds. Breast Diseases. 2nd ed. Philadephia,Pa: JB Lippincott Co; 388-419, 1991.

10. NIH Consensus Conference. Treatment of early-stage breast cancer. JAMA, 265: 391-395, 1991.

11. Haffty BG: Follow-up and Salvage Therapy for the Conservatively Treated Breast Cancer Patient. Se, in Rad Onc 2: 132-139, 1992.

12. Kurtz JM, Amalric R, Brandone H etal: Local Recurrence after breast-conserving surgery and radiotherapy. Frequency, time, course, and prognosis. Cancer 63: 2217-2225, 1989.

13. Fourquet A, Campana F, Zafrani B et al: Prognostic factors of breast recurrence in the conservative management of early breast cancer: A 25 year follow-up. Int J Radiat Oncol Biol Phys 17: 719-725, 1989.

14. Fowble B, Solin LJ, Schultz DJ, et al: Breast recurrence following conservative surgery and radiation: Patterns of failure, prognosis, and pathologic findings from mastectomy specimens with implications for treatment. Int J Radiat Oncol Biol Phys 19: 833-842, 1990.

15. Recht A, Schnitt SJ, Connolly JL et al: Prognosis following local or regional recurrence after conservative surgery and radiotherapy for early stage breast carcinoma. Int J Rdiat Oncol Biol Phys 16: 3-9, 1989.

16. Abner. AL, Recht A, Eberlein T etal: Prognosis Following Salvage Mastectomy for Recurrence in the Breast After Conservative Surgery and Radiation Therapy for Early-Stage Breast Cancer. Jnl of Clin Onc 11: 44-48, 1993.

17. Haffty BG, Fischer D, Beinfield etal: Prognosis following local recurrence in the conservatively treated breast cancer patient. int J Radiat Oncol Biol Phys 21: 293-298. 1991.

18. Clarke DH, Le MG, Sarrazin D et al: Analysis of local-regional relapses in patients with early breast cancers treated by excision ans radiotherapy: Experience of teh Instistut Gustave-Roussy. Int J Radiat Oncol Biol Phys 11: 137-145, 1985.

19. Haffty BG, Toth M, Flynn S t al: The prognotic value of DNA flow cytometry in eth locally recurrent conservatively treated breast cancer patient. Int J Radiat Oncol Biol Phys 21: 132, 1991 (abstr).

20. Aberizk WJ, Silver B, Henderson IC et al: The use of radiotherapy for treatment of isolated locoregional recurrence of breast carcinoma after mastectomy. Cancer 58:1214-1218, 1986.

21. Robinson DW. Surgical Problems in the Excision and Repair of Radiated tissue. Plast Reconsrt Surg 55: 41-48.

22. Osborne, MP, Borgen, PI, Wong, Gy etal: Salvage Mastectomy for Local and Regional Recurrence After Breast-Conserving operation and Radiation Therapy. Surg, Gyn, and Obst, 174:189-194; 1992.

23. Barr LC, Phillips, RH, Brunt AM, et al: Salvage Mastectomy after Failed Breast-conserving therapy for carcinoma of the breast. Annls of the Royal Col of Srgns of Eng, 73: 126-129; 1991.

24. Cacujum, CC, Tsangaris, TN, Nemoto, T et al: Results of Salvage Mastectomy for Loca Recurrence after Breast-Conserving Surgery without Radiation Therapy. Cancer, 71: 1774-1779; 1993.

25. Hathaway CL, Rand, RP, Moe R et al: Salvage Surgery for Locally Advanced and Locally Recurrent Breast Cancer. Arch Surg, 129:582-586; 1994.

26. Dickson MG, Sharoe DT. The complications of tissue expansion in breast reconstruction: a review of 75 cases. British Journal of Plastic Surgery, Vol 40, 629-635, 1987.

27. Evans GR, Schusterman MA, Kroll, SS et al. Reconstruction and the radiated breast: is there a role for implants? Plast Reconstr Surg, Vol 96, 1111-1115, 1995.

28.Spear SL, Maxwell GP. Discussion: reconstruction and the radiated breast: is there a role for implants? Plast Reconstr Surg. Vp; 96., 1116-1118, 1995.

29. Kroll S, Schusterman MA, Reece GP, et al: Breast Reconstruction with myocutaneous flaps in previously irradiated patients. Plast. Reconstr. surg. 93: 460, 1994.

30. Forman, D, Chiu J, Restifo, R, Ward, BA, Haffty, B, and Ariyan, S. Breast Reconstruction in Previously Irradiated Patients Using Tissue Expanders and Implants: A Potentially Unfavorable Result. Annals of Plastic Surgery, Vol 40, No 4, 360-364, 1998.

31. Fodor PB, Swistel AJ. Chest wall deformity following expansion of irradiated soft tissue for breast reconstruction. NY State J Med 89: 419-429, 1989.

HARVEY CUSHING / JOHN HAY WHITNEY
MEDICAL LIBRARY

MANUSCRIPT THESES

Unpublished theses submitted for the Master's and Doctor's degrees and deposited in the Medical Library are to be used only with due regard to the rights of the authors. Bibliographical references may be noted, but passages must not be copied without permission of the authors, and without proper credit being given in subsequent written or published work.

This thesis by has been used by the following persons, whose signatures attest their acceptance of the above restrictions.

NAME AND ADDRESS DATE

YALE MEDICAL LIBRARY

3 9002 01006 3759